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NEUTRALIZING BRAIN-DERIVED NEUROTROPHIC FACTOR AND FOCAL APPLICATION OF FIBROBLAST GROWTH FACTOR 2 INTO PARALYZED VIBRISSAL MUSCLES PROMOTE BETTER REINNERVATION AND RECOVERY OF WHISKING AFTER FACIAL NERVE INJURY IN RATS

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Introduction. After facial nerve injury in rats, recovery of vibrissal whisking is associated with a high proportion of mono-innervated neuro-muscular junctions (NMJ); poor recovery is associated with a high proportion of poly-innervated NMJ. Although excessive sprouting of the terminal Schwann cells (TSCs) is thought to promote poly-innervation, the molecular mechanisms underpinning TSC-sprouting are poorly understood. Denervated muscles produce various short-range diffusible sprouting stimuli, some of which have been identified as trophic factors. We recently quantified mRNA and protein levels of brain derived neurotrophic factor (BDNF) and fibroblast growth factor-2 (FGF2) in denervated vibrissal muscles in two rat strains: Sprague Dawley (SD)/RCS rats that are blind due to photoreceptor degeneration, which restore vibrissal whisking spontaneously after facial nerve transection and anastomosis (FFA), and SD-rats with an intact visual system but poor recovery of whisking after FFA. In the vibrissal muscles of SD/RCS rats, but not SD-rats, there was an early increase in FGF2 at 2 days after FFA, followed by a late rise in BDNF at 28 days. We hypothesized that the early increase of FGF2 promoted rapid elongation and minimal branching of regenerating axons with a possible reduction in NMJ-polyinnervation and improved functional recovery.

Main part. Here, we investigated the effects of injecting paralysed vibrissal muscles with different concentrations of BDNF, anti-BDNF and FGF2 at different postoperative periods after facial (*r. buccalis*) nerve transection and anastomosis (BBA). We found that regardless of treatment, the range of vibrissal movements remained impaired two months after BBA. Nevertheless, the combination of presumed initial post-injury blockade of axonal regrowth with anti-BDNF and presumed fostering of elongation in groups with high-dose FGF2 promoted better restoration of motor performance. Accordingly, we observed relatively good recovery in three groups of rats which received (i) anti-BDNF, (ii) anti-BDNF + FGF2 and (iii) FGF2. Since the degree of NMJ-polyinnervation, in group anti-BDNF + FGF2 was lowest than that in the other groups, our results indicate that the best therapeutic combination, which promotes best recovery of amplitude and lowest degree of polyinnervation, is a combination of anti-BDNF and FGF2.

Conclusions. We conclude that, after peripheral nerve injury and surgical repair, appropriate target reinnervation, and therefore function, can be restored by administering different trophic factors, but that they need to be applied over a specific time course and at specific concentrations.